

REMARKS

Claims 2-4, 16-18, 24, 25, 27-30, 32, 33 and 35-40 were pending in this application. Claims 28 and 29 are now cancelled without prejudice to Applicant's right to prosecute their subject matter in the present application and in related applications. Claim 30 is amended without any intent of disclaiming equivalents thereof. New claim 41 is added. Accordingly, claims 2-4, 16-18, 24, 25, 27, 30, 32, 33 and 35-41 are pending and presented for consideration.

Claim Amendments

Support for amendments to claim 30 is found in the specification at least, for example, at page 12, lines 31-34, and at page 13, lines 13-21. Support for new claim 41 is found in the specification at least, for example, at page 35, lines 10-12.

Applicant submits that the amendments to the claims introduce no new matter.

Claim Rejections under 35 U.S.C. § 103 over Sytkowski et al. (WO 99/02709) in view of U.S. Patent No. 6,608,183 to Cox

Claims 2-4, 16-18, 24, 25, 27-30, 32, 33, 35 and 39 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sytkowski *et al.* (WO 99/02709) in view of U.S. Patent No. 6,608,183 to Cox ("Cox"). Applicant respectfully traverses the rejection to the extent it is maintained over the claims as amended.

The appropriate criteria for the determination of obviousness under 35 U.S.C. § 103 is whether the prior art would have suggested to one of ordinary skill in the art that the claimed subject matter should be carried out and would have a reasonable likelihood of success. Both the suggestion and the expectation of success must be founded in the prior art, not in Applicant's disclosure. *In re Dow Chemical Company*, 837 F.2d 469,473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). That is, obviousness cannot be established by combining the teachings of the prior art to produce claimed invention, absent some teaching or suggestion or incentive in the art supporting the combination. *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Cited references which merely indicate the isolated elements recited in the claims are not a sufficient basis for concluding that the combination would have been obvious. *Ex parte Hiyamaizu*, 10 U.S.P.Q.2d 1393 (BPAI 1988).

Applicant submits that even if the disclosures of Sytkowski and Cox were combined, such combinations would not teach Applicant's invention as claimed in amended independent claim 30. Amended independent claim 30 relates to an Fc-erythropoietin (Fc-EPO) fusion protein and requires that the erythropoietin (EPO) portion have a substituted Cys at a position corresponding to Gln₈₆, Pro₈₇, Trp₈₈, Glu₈₉, or Leu₉₁ of human EPO and an amino acid other than Cys at a position corresponding to position 33 of human EPO so that the substituted Cys may form a disulfide bond with a Cys corresponding to position 29 of human EPO. Sytkowski does not teach or suggest cysteine variations in EPO protein. Cox does not teach the cysteine variations as claimed in claim 30. In fact, Cox teaches away from the claimed invention. Cox relates to modified growth hormones, including EPO, with added or created free cysteines for site-specific conjugation of the modified growth hormones with polyethylene glycol (PEG) or other such moieties (*see, e.g.*, column 3, lines 49-52). In particular, as set forth on column 4, lines 1-11, Cox states: "The preferred method for PEGylating proteins is to covalently attach PEG to cysteine residues using cysteine-reactive PEGs. . . . At neutral pH, these PEG reagents selectively attach to 'free' cysteine residues, i.e., cysteine residues not involved in disulfide bonds." [Emphasis added.] In order to introduce free cysteines into EPO protein, Cox teaches adding free cysteines at certain amino acid positions including position 88 (*see, e.g.*, Cox, column 3, lines 13-27, and column 26, lines 45-51). Alternatively, as set forth on column 25, lines 59-64, Cox teaches: "A 'free' cysteine can be created by changing either cysteine-29 or cysteine-33 to another amino acid. Preferred amino acid changes would be to serine or alanine. The remaining 'free' cysteine (cysteine-29 or cysteine-33) would be a preferred site for covalently modifying the protein with cysteine-reactive moieties." [Emphasis added.] Therefore, although Cox teaches cysteine substitution at position 88 or changing cysteine-33 to a non-cysteine amino acid as alternative embodiments to generate free cysteines, Cox does not teach or suggest a combination of a substituted cysteine at position 88 and a non-cysteine amino acid at position 33 so that the substituted cysteine may form a disulfide bond with a cysteine corresponding to position 29 of human EPO as required by amended claim 30. Nor would Cox provide any motivation or incentive to one of skill in the art to combine a substituted cysteine at position 88 with a non-cysteine amino acid at position 33 so that the substituted cysteine may form a disulfide bond with a cysteine corresponding to position 29 of human EPO. Thus, even if

the disclosures of Sytkowski and Cox were combined, such combinations would not teach Applicant's invention.

Applicant therefore respectfully submits that independent claim 30 and the claims dependent therefrom are novel and unobvious over the cited references and request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claim Rejections under 35 U.S.C. § 103 over Sytkowski et al. in view of Cox and in further view of U.S. Patent No. 5,888,772 to Okasinski et al.

Claim 29 stands rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sytkowski *et al.* in view of Cox and in further view of U.S. Patent No. 5,888,772 to Okasinski *et al.* ("Okasinski"). Applicant has cancelled claim 29 without prejudice and without acquiescing to the rejection. Therefore, the rejection with respect to claim 29 is moot.

Claim Rejections under 35 U.S.C. § 103 over Sytkowski et al. in view of Cox and in further view of U.S. Patent No. 5,585,097 to Bolt et al.

Claims 36-38 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sytkowski *et al.* in view of Cox and in further view of U.S. Patent No. 5,585,097 to Bolt *et al.* ("Bolt"). Applicant traverses the rejection.

Claims 36-38 depend directly or indirectly from independent claim 30, therefore, incorporate by reference all limitations of claim 30. As argued above, even if the disclosures of Sytkowski and Cox were combined, such combinations would not teach the invention as claimed in independent claim 30 and its dependent claims including 36-38. Bolt does not correct the deficiencies of Sytkowski and Cox because the teachings of Bolt are irrelevant to the cysteine variations in EPO protein. Therefore, even if the disclosures of Sytkowski, Cox and Bolt were combined, such combinations would not teach the Applicant's invention.

Applicant therefore respectfully submits that claims 36-38 are novel and unobvious over the cited references and request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully submits that pending claims 2-4, 16-18, 24, 25, 27, 30, 32, 33 and 35-41 are in condition for allowance. The Examiner is invited to telephone the undersigned agent to discuss any remaining issues.

Respectfully submitted,



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